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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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EDITORIAL

A FORGOTTEN AND UNDERPRIVILEGED MINORITY

FOR some years now, we have heard repeatedly of minority rights and how the underprivileged should be given proper regard and protection in a true democracy such as ours is supposed to be. We hold no argument against such philosophy and we surely feel resentful when we see the rights of some of our minority groups being transgressed. There is, however, a minority group in the United States, today, to whom scant attention is paid, particularly by those mass media of entertainment: radio and television. Since the editor belongs to this minority and has little opportunity to express his resentment, he is doing so here. It is with the full realization, of course, that it will do little good except to give him the opportunity of giving vent to his pent-up emotions and utter disgust at the trend which shows no sign of lessening.

Practically all of our radio and television programs are underwritten by sponsors who have a product to sell, and who wish to promote its sale to the largest possible number of potential customers, using radio and television as mass media of selling. It is quite understandable that in selecting programs they do so after a careful survey of what is likely to appeal to the majority of listeners or viewers. As a result, television and radio programs in the main are scaled down to the least common denominator, insofar as public intelligence and artistic appreciation is concerned. In the past decade, it has been tragic to see television deteriorate just as did radio some few decades before. Now that even the unemployed and those on public assistance consider a television set a necessity and almost everyone, regardless of economic status, has one, this medium has become largely saturated with cowboy, hillbilly, rock and roll, and give-away programs. There is no question that this is what the large mass of the general public wants and those who have products to sell continue to pour out on the public at large this low-grade, lowbrow entertainment.

While those who would enjoy a somewhat higher level type of program are indeed in a minority, they are an almost completely for-

gotten minority. There are times when it is practically impossible to find any program at all on radio or television except this cheap, tawdry portrayal of murder, sex, and crime interspersed with some commercial wherein the "sales-pitch" is done by some "character" who almost screams his blatant story until it can be heard in every nook and cranny of the house. Those patient and long-suffering citizens who resent this clamor and superficiality find some surcease in books and good recordings which they play in their homes while their radios and television sets sit mute and silent most of the time.

Occasionally, some station will try to provide—let us say—good music such as was done recently in Philadelphia on a newly formed AM station, but the Federal Communications Commission mindful of the wishes of the masses gives it only a very weak signal and one which just a few miles away is completely overpowered by the bedlam of stations giving the people what they think they want.

If, indeed, the damage stopped here and those of us who enjoy good music and mature programs were the only losers, it might not be too serious. Unfortunately, radio and television, have become largely, through parental neglect, the media for educating our youth. As a result, children grow up with the most superficial kind of training and, at times, an almost brutal and sadistic attitude toward society. Each evening, they can see several people "murdered" in cold blood and learn, just by watching, the best technique to dispose of their presumed enemy. Their musical tastes are distorted and perverted by bands and "combos" which play no music but an ear-jarring rendition, usually accompanied by torso-twisting and grimacing in a manner not too far removed from that of the African savage.

As one views this continuing trend in America and the philosophy that what the majority wants is both right and must be given them, one begins to doubt whether in the final analysis our brand of so-called democracy will in the long run triumph over some of those less democratic regimes which we depise. Those government agencies which theoretically are supposed to supervise such things are ruled entirely by expediency and consider radio and television stations just as any other business and free to sell that which is in demand. The minority of which we speak can do little else but survey the passing scene and reflect on what history teaches us happens in the final analysis when irresponsibility and the pursuit of the most superficial kind of diversion becomes the great national pastime. We can, of

course, be sure of one thing: our minority will grow smaller and smaller as the opportunity to see and hear the better things in life diminishes day by day for our children, and those who resent the trend are overwhelmed by public ridicule and derision at their failure to be "modern" and keep up with the times.

There is, of course, just an "outside" chance that, by their very excesses, radio and television may cease to be free to operate as they wish. There are some responsible people both in and out of government who are beginning to appreciate the significance of these media in influencing our national life and destiny. While we dislike regimentation, irresponsibility is worse. If government regulates the food and drug industries to prevent the poisoning of our bodies, it should give equal attention to the debasement and poisoning of our minds.

The ideal solution, of course, would be for those in the radio and television fields to recognize their heavy responsibilities in shaping public attitudes, morals, and appreciation for the finer things in life. They, more than anyone else, can change America from the jukebox, devil-may-care philosophy for which we are noted to something more substantial and more in keeping with our presumed position of world leadership.

L. F. Tice

A PRELIMINARY REPORT ON SOME NEW QUATERNARY AMMONIUM DERIVATIVES

By Rudolph Rebold,* Anthony J. Monte Bovi ** and Paul T. Medici **

THE ability possessed by certain of the newer synthetic phenolic compounds to reduce the bacterial flora of the skin, and to remain active thereon for considerable periods of time (1, 2, 3), has brought renewed interest in the search for more efficient bacteriostatic and bactericidal agents (4, 5, 6, 7). Of considerable interest is the adsorbent or substantive property of these newer synthetics which enables them to remain active for long periods of time on skin, animal, vegetable and synthetic fibers, and even on some metals (8, 9, 10).

The quaternary ammonium compounds have long been known to possess this interesting adhering property. However, the ease with which anionic agents, especially soaps, so easily destroys this substantive ability makes full exploitation of this valuable property impossible. Recently,* a group of chemicals were synthesized by replacing the halide of a quaternary ammonium compound with other groups which also possessed inherent germicidal activity. Sixty such compounds were synthesized, the halide of the quaternary compound being replaced with the following groups,

1. Dithiocarbamate
2. Mercaptobenzothiazole
3. Mercaptobenzoate
4. Naphthalene and Naphthol sulfonate
5. Phenol sulfonate
6. Benzosulfimide
7. Aminophthaleins.

While originally intended as agricultural fungicides, many of these compounds showed properties indicating their use as topical

* Gallowhur Chemical Corporation, Ossining, N. Y.
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bactericidal and bacteriostatic agents. One of these, lauryl dimethyl 3,4-dichlorobenzyl ammonium 2-mercaptobenzothiazolate ($C_{12}H_{25}$-$(CH_3)Cl_2C_6H_5CH_2N.C_6H_4SCSHN$), shows the most promise in possessing all of the desirable substantive and bacteriostatic properties of the quaternaries, even in an anionic environment. The following properties have already been established for this compound:

Physical Properties

1. *Description:* Light yellow crystalline, non-volatile solid, somewhat waxy to the touch.
2. *Solubility:* Insoluble in water. Slightly soluble in benzene and chloroform. Freely soluble in acetone, lower alcohols, and lower glycols.
3. *Stability:* Good. No change in clear, colorless glass bottles over a simulated 3 years storage under normal conditions.
4. *Melting Point:* 111° C.-114° C.
5. *Molecular Weight:* 561.7.

Toxicity

Preliminary toxicity studies on rats shows the fatal dose lies between 500-5000 mg./Kg. This represents a comparatively low order of toxicity when compared to other quaternaries already approved for restaurant use.

Biological Activity

Test Organism	Bacteriostatic (11)	Bactericidal (11)
Aerobacter aerogenes	1-5000	1-1000
M. pyogenes var. aureus	1-100,000	1-50,000
Salmonella typhosa	1-10,000	1-1000
Escherichia coli	1-100,000	1-1000
Proteus vulgaris	1-1000	under 1-1000
Pseudomonas fluorescence	over 1-500,000	over 1-500,000
Bacillus Megatherium	over 1-500,000	1-100,000
Bacillus mycoides	1-100,000	1-100,000
Bacillus subtilis	over 1-500,000	1-100,000

Fungistic Activity (12)

200 ppm. against Aspergillus niger, on potato dextrose agar.

Indicated Phenol Coefficient (11)

Test Organism	Value
M. pyogenes var, aureus	375
Salmonella typhosa	125
Aerobacter aerogenes	143
Bacillus mycoides	353

The possibility that this quaternary would retain its bacteriostatic activity in contact with soap was investigated. A soap base containing 2% of the quaternary was prepared and tested against, (1) the base soap alone. (2) A commercially available soap containing a non-quaternary bacteriostat. (3) A commercially available soap containing an inorganic mercurial. Zones of inhibition were compared on agar plates inoculated with M. pyogenes var, aureus (13). Preliminary results show the following:

Soap Used	Zone of Inhibition
#1	0.5 cm.
#2	1.0 cm.
#3	1.3 cm.
#4 (sample)	1.1 cm.

This development is being investigated further to test the substantive or adsorbent power of such soaps.

Summary and Conclusion

A series of quaternary ammonium compounds have been synthesized. These substances are unusual since they seem to possess bacteriostatic activity even in the presence of anionic agents, such as soaps.

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YOUR FUTURE DEPENDS ON YOU! *

By Rudolph H. Blythe

IT is a real honor for me, an alumnus, to be able to participate in your graduation exercises. Many of you probably have mixed emotions similar to those that I experienced 27 years ago when I sat where you now sit—relieved that my academic training was behind me. Yet, I had a profound desire to go on . . . and attack the next challenge.

One's college life is so busy with study, extra-curricular activities, and outside work that one has little chance to take a panoramic view of the future. It is, therefore, the privilege and responsibility of the commencement speaker to take time to peer into the crystal ball and explain briefly to the graduating class what is seen. I hope it helps you in the coming years.

Prophesying on the immediate future is largely a matter of studying trends, then projecting or extrapolating these data. The next 10-15 years are ones that are going to be the most important to you, as it is during this period that you will form your life patterns. I should be on reasonably sound ground for that short a time, and need not be as imaginative as Jules Verne.

I can only give you a picture of the trends. *What you do* and where you fit into this overall picture *depends upon you.* You see, I am a strong believer in the old adage . . . "that each man largely directs his own destiny by what he does and what he makes of himself."

Probably all of us have seen Westerns at one time or another in which a cowboy was riding with a stampeding herd; by going with it, he could gradually force the herd to the left or right. Had he tried to stand still, he would have been run down . . . trampled. So it is in our lives. We can effectively change trends or practices to our advantage by riding with them, and at the same time exerting strong tangential forces in the direction we desire to go. If we stand still,

* Commencement Address at the Albany College of Pharmacy on June 12, 1958. Dr. Blythe is Director of Pharmaceutical Research, Smith Kline & French Laboratories, Philadelphia, Pa.

or fail to take positive action, we will be submerged and swept along with the trends—never achieving the goal of our choosing. Suppose we illustrate this with a pharmaceutical example. Our pharmacy is located in an area where most of the physicians dispense. It would be a formidable task to make them abruptly stop dispensing. However, we can take advantage of the trend toward the increased use of new potent specifics which are more expensive than the dispensers old armamentarium of aspirin and compound white pine cough syrup, work with dispensers and gradually educate them to the habit of prescribing. It will take tact, patience and hard work, but it can be done. I could cite numerous other examples, but let me try to point out the trends as I see them and you can decide what your aims are and how you can take advantage of these trends to achieve your goals.

We are all interested in some facet of pharmacy and will play an essential part on the health team whether we dispense medication in the retail capacity, acquaint the physician with it as a professional service representative, or create and manufacture it in an industrial capacity. Statistics indicate that about 80% of you will practice retail pharmacy, so I shall concentrate most heavily on that phase, looking first at the overall picture and then focusing in greater detail upon retail work.

When plotting a line or course, one must use many points, but after it has been charted, one needs only to describe key points to show the general direction of that course. Similarly, it has been necessary to make a detailed study of trends in order to visualize the probable developments in pharmacy during the next few years. However, I now need only to describe a few key periods so that you can see the general direction of these trends.

At the turn of the century, the independent pharmacist prepared many galenicals in his back room—in his own miniature manufacturing area. The pharmacist sold these preparations over the counter as well as using them in the limited number of prescriptions that he filled. And a considerable amount of crude drugs were also sold by the ounce to people to make their own teas and decoctions at home. Most medication was relatively mild in comparison to many of our potent synthetics of today. Furthermore, most were used as palliatives to relieve symptoms rather than to cure a specific infection or disease. The techniques of diagnosis were just as general and ill-defined as were our therapeutic preparations.

By 1930, the sale of crude drugs had diminished to a trickle. Large manufacturers like Lilly and Parke-Davis were selling galenicals in gallons to the retail pharmacist to package and to use in compounding prescriptions. Proprietary preparations were increasing in number and volume. Medicine, too, had advanced. Insulin had been found to be effective in treating diabetes, and liver extracts were being prepared to treat pernicious anemia. Research was in its infancy both in medicine and in the pharmaceutical sciences. Now that specifics had been found for diabetes and pernicious anemia, the drive had started to overcome disease after disease.

You are all aware, of course, of the successive discoveries of many of the specifics since that time—sulfonamides, amphetamines, antibiotics, synthetic antispasmodics, steriods, phenothiazines and vaccines.

In 1930, the research departments consisted mostly of a few chemists and an occasional pharmacologist, but rarely a pharmacist. Today, most laboratories are highly integrated team operations employing at least 6 and sometimes as many as 15 types of scientific specialists, depending upon the size of the laboratory and the degree of specialization. Today, pharmacy is a key member of the team.

At Smith Kline & French, for example, our research division has grown from 3 people in 1930 to over 700 people with a research budget of about 10 million dollars for 1958. The drug industry is now reinvesting over 125 million dollars of its annual earnings in research. The government's National Institute of Health is spending over $200 million, largely on basic research. Foundations, like those for tuberculosis, cancer, and heart, are spending additional millions.

This investment in research has paid high dividends in health and in life—our lives. Life expectancy at birth has increased from 48 years in 1900 to over 69 years in 1958. Just since 1939, when most of this graduating class were infants, the life expectancy at birth has increased about 7 years. During this same period of less than 20 years, mortality from pneumonia has been reduced 61%, and appendicitis 76%.

The alarmist might ask . . . "Will all of this research and the decrease in death rate eventually wipe out disease and the pharmacy?" The answer is definitely No! During this same 20 year period, when mortality has been decreasing, retail pharmacy sales have soared from 169 million to 1.5 billion—nearly a 10-fold increase. In 1939, less than 12% of pharmacy's sales were in prescriptions, while last year over

25% of its business was in prescriptions. This accounted for 40% of the pharmacist's profits. And it is reasonable to expect that our prescription dollar volume will double during the next ten years. This will probably be due to the combined effect of an increased number of prescriptions and these at a continuing higher cost. The increased number of prescriptions is due to both an increased population and a greater emphasis upon preventive medicine. More people are going to their physicians for annual or periodic check-ups. Statistics show that each visit to the physician represents 1.7 prescriptions. And we can help our customers and ourselves by encouraging this trend.

Let's digress a bit to consider the gradual increase in the cost of prescriptions, as it is an important public relations factor that both the manufacturer and the retailer must face squarely. When it is so treated, it is seldom a problem. Our customers don't know, and sometimes we do not realize, that less than ½ of 1% of all prescriptions cost over $10, and that over 50% cost less than $2. Even with the occasional expensive prescription, the patient continues to receive a tremendous bargain due to the increased efficacy of the medication. We have no cause to be self-conscious or embarrassed.

But the patient is not usually placated by being informed that the higher prescription cost is due to the continuing increase in cost of medical research and the greater complexity of syntheses and control procedures. The most convincing way that we can show him that he is getting the best bargain available is to give him the actual facts on dollars saved. One can illustrate with any of a number of diseases that today's newer, more effective medications shorten the course of the illness and provide savings through less time lost from work, shorter periods in the hospital and fewer visits by the physician. However, to some, the most important benefit is the decrease in the mortality rate and the substantial deferment of that inevitable day when we meet our Maker. By the way, we must remember that the customer is either sick himself, or that someone in his family is sick, and that this probably has a depressing effect upon him. Naturally, he would much rather be spending this money on a steak dinner or a ballgame than he would on a physician's visit and a prescription. This is a real opportunity for you to utilize your best professional and "prescription-side" manner.

What Other Factors Will Affect the Practice of Pharmacy?

1. There is an increase in population—at the rate of nearly two million per year. This is the result of increased birth rate, decreased mortality rate and continued immigration. More people mean more drug consumption.

2. On the negative side, there are more supermarkets and these are syphoning off some of the sales of toiletries and a few other over-the-counter items.

3. There is a change of shopping patterns—better roads take rural people to more urban areas, and urban people with more money to spend are migrating to the suburbs. There is a trend toward shopping centers, each usually having its pharmacy. In the cities, physicians continue to concentrate in office buildings or areas with prescription stores in the neighborhood. Each of you will have to study what effect any of these changes might have on pharmacy in your community.

4. Pharmacists in general desire shorter hours. The number of new pharmacists and pharmacies is not increasing at the same rate as is the population.

The decrease in the ratio of pharmacists to the total population, the pharmacist's desire for shorter hours per day and per week, and the continued increase in the percentage of the pharmacy's sales in the form of prescriptions are all factors which will result in a decrease in the "one-man" store and an increase in the number of "two-man" or even larger stores. Furthermore, there will be an increase in the pharmacist's salary and this will make it increasingly uneconomical for him to use his time selling merchandise that can be handled by people with less education. All of these factors tend toward an increase in the utilization of the pharmacist's time for professional work.

Most of these trends can be directed to your advantage. To accomplish this, you should choose the type of store that you wish—prescription, general or merchandising—and then select the type location and personnel best suited to it, taking the trends into account. However, if location happens to be the most important factor to you, you would be well advised to study the trends in that neighborhood and develop the type store suited to these.

Our personality characteristics, both good and bad, strongly influence our chance of success. There is probably no field in which the ideal characteristics are more important than in retail pharmacy. They affect the rapport that one establishes with his customers, the professional atmosphere of the store, and the very drive with which both professional and business aspects are pursued. While personality depends to a large extent on our heritage and early life, we can, by diligent effort, strengthen our assets and submerge our liabilities.

The traits that I would encourage you to develop are:—a genuine interest in people, neatness, ingenuity, ambition, perseverance, and an altruistic civic-mindedness. Above all, I urge you to develop your creativity to its fullest. Not only is it exceedingly important, but it is probably one of the easiest of all of our native talents to develop. There is no field in which we do not need creativity. You will find the same approach successful in retail pharmacy that we do in research. This approach is—take time to analyze the problem critically—whether it involves store layout or personnel relations; then think of all possible approaches that you can of attacking the problem. Having done this, temporarily discontinue active thinking on the problem and let the ideas incubate in your subconscious. A little later, rethink the problem through, and the best approaches will crystallize, and you can drive them into action. The biggest deterrents to productive creativity are negative thinking and the fear of doing something unconventional . . . something that has not been done before.

The examination that I have made of pharmacy reaffirms my faith in its future. All branches look good—but each needs to be approached thoughtfully, sincerely and energetically—you can make your future what you will.

Good luck and good pharmacy!

RE-THE DISPENSING PHYSICIAN *

By F. P. Rhoades, M.D.

FROM the beginning of the history of medicine, the physician has not only carried his medicaments with him but has also maintained a stock in his office. Until 1240 A. D., he combined the functions of both physician and pharmacist; collecting medicinal herbs and compounding his prescriptions.

The passage of time has witnessed the overwhelming multiplication and diversification of therapeutic agents. Within the memory of many physicians and pharmacists, the multi-ingredient prescription flowered; reached its zenith, then declined to its nadir. Practically every combination of drugs that has a rational use in treatment is marketed in a stable and attractive pill, capsule, powder, ointment, lotion, or liquid. They are in essence prefabricated prescriptions that require little skill in dispensing, and only need to be taken from a stock bottle.

Due to the absence of competent pharmacists in some isolated localities, the necessity for total dispensing by a few physicians still remains. However, the vast majority practice in areas served by well trained pharmacists. Thus, total dispensing today is no longer only for the convenience of the patient, it has an economic motivation. The traditional reluctance of the physician to raise his base fee, has resulted in the dispensed medication becoming the pretext for an increase, thus making it necessary to dispense on every visit of the patient. The physician should have the courage to charge a realistic fee for his professional services that is not contingent upon added benefits such as total dispensing represents. Of course, a minimum amount of dispensing, such as giving the patient sufficient medication to last until he has the opportunity to have the prescription filled, represents a real service.

The type of total dispensing engaged in by many physicians today is both unprofessional and unethical. Unprofessional since a portion of the fee charged is not for medical services and, unethical as the

* Reprinted from the July, 1957, Bulletin of the Wayne County and Michigan Academies of General Practices.

best interests of the patient are not being served. The basis of dispensing being economic, the less expensive medications are usually stocked. This deprives the patient of the benefits of the products of research that are necessarily more expensive. In the absence of the indicated agent it often leads to substitution. Thus the ultimate is frequently reached—the substitution of a substitute for a substitute!

The specter of some form of state medicine still hangs over us, and we need the support of all members of the health-team, especially the pharmacist whose contacts with the public are frequent and intimate. His continuing support will depend upon benefits derived from, and identification with, the private practice of medicine.

The "counter-prescribing" we have long decried is frequently the direct reaction to "office dispensing". In order to survive in a community where many physicians practice total dispensing, pharmacists are forced to merchandise a plethora of non-medical items. If the traditional relationship between pharmacy and medicine is to be maintained, there must be a re-emphasis on cooperation and a mutual respect for each other's fields of endeavor.

The private practicing physician is the logical one to champion such a mutually beneficial partnership which, fortuitously and necessarily if it is to endure, coincides with the best interests of the public.

STUDIES OF THE GENUS THYMUS
PART VIII

Comparison of the Floral Leaves and Calyces of the Various Species of Thymus

By Ikram Hassan * and M. S. Dunn **

IN the present paper, an attempt has been made to compare the relative sizes and appearances of the floral leaves and the split and spread out calyces of twelve Thymus species studied and reported in previous papers.

Method of Study

The floral leaves and calyces examined in this study were obtained from the same samples used in the histological work reported earlier. These plant parts were prepared for examination as described in our paper (1).

The floral leaves and calyces when ready for observation were placed on the stage of the Bioscope and their images were projected on drawing paper placed at a fixed distance. A drawing was made in each case from the projected image.

The magnification was determined directly by comparing the actual length in mm. and the length in mm. of the drawing.

Summary

The drawings of the twelve floral leaves are shown in Figs. I and II, while those of the calyces are presented in Figs. III and IV.

As may be seen from study of these figures, the shapes and sizes of the floral leaves and calyces are variable. The marginal trichomes, (used by Hocking (2) in describing Mentha cardiaca) also present a striking histological characteristic of value in the comparative study of some Thymus species.

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** Professor of Biology and Director of the Biology Department, Philadelphia College of Pharmacy and Science, Philadelphia, Pa.

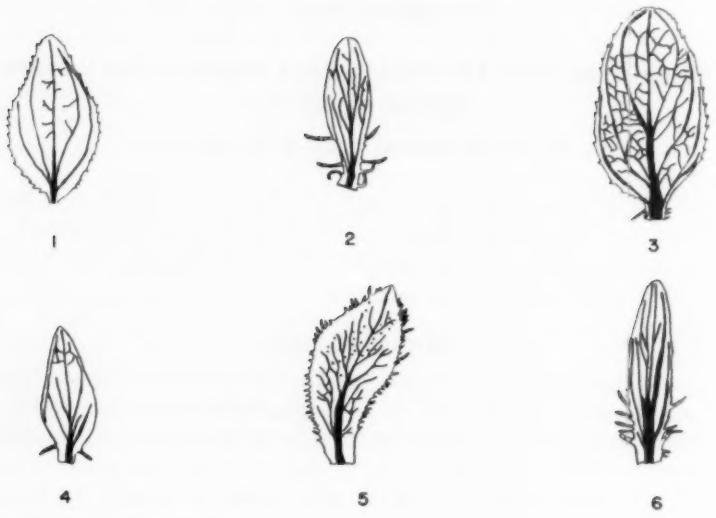
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FIGURE I

FLORAL LEAVES OF VARIOUS SPECIES OF THYMUS STUDIED

1. Thymus vulgaris.
2. Thymus Serpyllum.
3. Thymus Chamaedrys.
4. Thymus Herba-barona.
5. Thymus capitatus.
6. Thymus striatus.

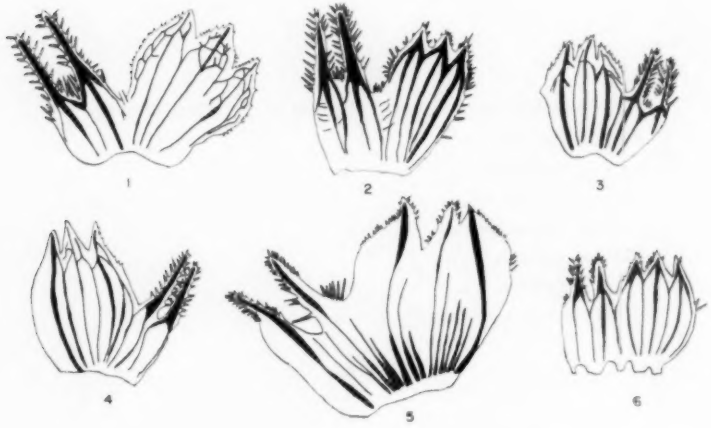
Bioscope drawings. Magnification approx. 4X.

FIGURE II

FLORAL LEAVES OF VARIOUS SPECIES OF THYMUS STUDIED

7. Thymus carnosus.
8. Thymus villosus.
9. Thymus hirsutus.
10. Thymus heterotrichus.
11. Thymus pectinatus.
12. Thymus Zygis.

Bioscope drawings. Magnification approx. 4X.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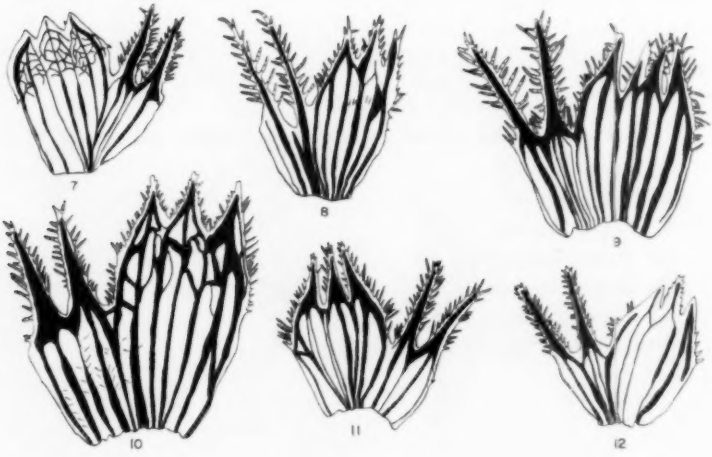
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FIGURE III

CALYCES OF VARIOUS SPECIES OF THYMUS STUDIED

1. Thymus vulgaris.
2. Thymus Serpyllum.
3. Thymus Chamaedrys.
4. Thymus Herba-barona.
5. Thymus capitatus.
6. Thymus striatus.

The calyces were split open, and placed on a slide, in chloral hydrate, with the outer surface uppermost. Bioscope drawings. Magnification approx. 6X.

FIGURE IV

7. Thymus carnosus.
8. Thymus villosus.
9. Thymus hirsutus.
10. Thymus heterotrichus.
11. Thymus pectinatus.
12. Thymus Zygis.

The calyces were split open, and placed on a slide, in chloral hydrate, with outer surface uppermost. Bioscope drawings. Magnification approx. 6X.

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(1) Hassan, Ikram and Dunn, M. S., "Comparison of the Diagnostic Microscopical Characteristics of Thymus Chamaedrys Fries and Thymus Herba-barona Loisel," *Am. Jour. of Pharm. 130:*86-92 (1958).

(2) Hocking, G. M., "Scotch Mint and Spearmint: A Comparative Study of Cultural, Morphological, and Histological Characteristics of Species of Mentha Growing in Florida, III," *Jour. Am. Pharm. Assoc., Science edition 37:*394-402 (1949).

STUDIES OF THE GENUS THYMUS
PART IX

Tabulated Histological Data for Certain Thymus Species

By Ikram Hassan * and M. S. Dunn **

TABLE I is a summary of the comparative histological structures of the twelve Thymus species discussed in our earlier papers.

The following characteristics were commonly found in almost all the species of Thymus studied:

Floral Leaf

The upper and lower epidermis were found to be straight or wavy walled, beaded and with cuticular striations. The nonglandular and glandular hairs or their scars on the two leaf surfaces of the species studied varied in amount.

The transverse section of the floral leaves in addition to the upper and lower epidermis, in a few cases, showed hypodermal cells; palisade tissue was present in nearly all the species; spongy parenchyma was present in all the species studied.

Stem

The epidermis of the stem showed straight walled (beaded or unbeaded walls) cells, with or without striated cuticle. Variously distributed trichomes or their scars were present.

Calyx

Outer Epidermis. The epidermal cells of the rib region invariably showed wavy, beaded walls with striated cuticle. Nonglandular and glandular trichomes were generally present.

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In the rib region, the cells had thin walls, and the cuticle showed striations; in some species, cell walls were raised to striated papillae.

In the divided region of the calyx tube, the epidermal cells had wavy walls and striated cuticle. Stomata were present.

Inner Epidermis. The tubular region showed cells with thin, wavy walls with cuticular striations. In the throat of the calyx were nonglandular hairs of different sizes (depending on the species) arranged in a circle in all the species studied.

In the divided region, the structure of the epidermal cells in most cases was identical with the divided region of the outer epidermis.

Marginal Hairs. The two narrower sepals possessed uniseriate 1-5 celled, stoutly built nonglandular hairs on their margins in nearly all the species studied, whereas in the three broader sepals, marginal trichomes were either lacking or varied from 1-5 cells in length.

Corolla

Outer Epidermis. The tubular region invariably showed long cells with very thin walls (wavy to straight). Usually 1-3 celled uniseriate nonglandular trichomes were found in all the species.

Inner Epidermis. In the tubular region, the cells were long and had very thin walls (wavy to straight). The trichomes were of several kinds: 1-3 celled nonglandular hairs (in almost all the species); 1-celled, club shaped nonglandular hairs with centrifugal projections; 1-celled, long, nonglandular hairs with shrunken walls (in some species).

The cells of the divided region always showed striated papillae.

TABLE 1

COMPARATIVE CHART SHOWING CHARACTERISTICS OF EACH SPECIES

PLANT PART	TISSUE	1. THYMUS VULGARIS LINN.	2. THYMUS SERPYLLUM LINN.	3. THYMUS CHAMAEDRYS FRIES	4. THYMUS HERBA-BARONA LOISEL	5. THYMUS CAPITATUS H. L.	6. THYMUS STRIATUS VAHL.
FLORAL LEAF	UPPER AND LOWER EPIDERMIS	CELL WALLS WAVY, OR STRAIGHT, BEADED, CUTICLE STRIATED; STOMATA PRESENT	CELL WALL WAVY, BEADED, CUTICLE STRIATED; STOMATA NOT ABUNDANT, OR STRAIGHT CELL WALLED EPIDERMIS AT PLACES	CELL WALLS WAVY, BEADED, CUTICLE STRIATED; STOMATA INFREQUENT	CELL WALLS WAVY, BEADED, CUTICLE STRIATED; STOMATA COMMON	UPPER EPIDERMAL WALLS WAVY, BEADED, LOWER EPIDERMAL WALLS STRAIGHT, BEADED CUTICLE STRIATED; STOMATA PRESENT	CELL WALLS WAVY, BEADED WALLS, CUTICLE WIDELY STRIATED; STOMATA PRESENT
	EPIDERMAL HAIRS	TRICHOMES AND TRICHOME SCARS IN ABUNDANCE	TRICHOMES AND TRICHOME SCARS SCARCE	TRICHOMES AND TRICHOME SCARS PRESENT	TRICHOMES AND TRICHOME SCARS IN ABUNDANCE	ON UPPER EPIDERMIS, TRICHOMES SCARCE. ON LOWER EPIDERMIS, TRICHOMES IN ABUNDANCE	TRICHOMES AND TRICHOME SCARS PRESENT
	HYPODERMIS	ABSENT	ABSENT	ABSENT	ABSENT	PRESENT (LIGNIFIED STONE CELL-LIKE)	ABSENT
	PALISADE TISSUE	ONLY UPPER PALISADE PRESENT	ONLY UPPER PALISADE PRESENT	ONLY UPPER PALISADE PRESENT	ONLY UPPER PALISADE PRESENT	UPPER AND LOWER PALISADE TISSUE PRESENT	ONLY UPPER PALISADE PRESENT
	PALISADE NUMBER	9.9	10.5	12.1	10.5	7.3	12.5
	STOMATAL COUNT	9.5	13.9	22.5	8.4	NOT DETERMINED	10.0
STEM	EPIDERMAL HAIRS	TRICHOMES AND THEIR SCARS ALL OVER THE EPIDERMAL SURFACE IN ABUNDANCE	TRICHOMES AND THEIR SCARS SCARCE. WHEN PRESENT, SCATTERED ALL OVER THE SURFACE	TRICHOMES AND TRICHOME SCARS ARRANGED IN FOUR ROWS IN ABUNDANCE	TRICHOMES AND TRICHOME SCARS ALL OVER THE EPIDERMAL SURFACE IN ABUNDANCE	TRICHOMES AND TRICHOME SCARS ALL OVER THE EPIDERMAL SURFACE IN ABUNDANCE	TRICHOMES AND THEIR SCARS ALL OVER THE EPIDERMAL SURFACE

PLANT PART	TISSUE	1	2	3	4	5	6
CALYX	EPIDERMIS OF OUTER TUBULAR REGION	INTERRIB REGION WITHOUT FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITH FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITH FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITH FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITHOUT FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITH FLUTED OR STRIATED PAPILLAE
	OUTER RIB REGION	FIBERS IN THE RIB REGION ABSENT	FIBERS IN THE RIB REGION ABSENT	FIBERS IN THE RIB REGION ABSENT	FIBERS IN THE RIB REGION ABSENT	FIBERS IN THE RIB REGION ABSENT	FIBERS IN THE RIB REGION ABSENT
	PALISADE LIKE CELLS IN DIVIDED REGION	ROUND IN SURFACE VIEW	ROUND IN SURFACE VIEW	ROUND IN SURFACE VIEW	ROUND IN SURFACE VIEW	UNLIGNIFIED, THICK WALLED WITH A CENTRAL LUMEN PALISADE TISSUE PRESENT	ROUND IN SURFACE VIEW
	HAIRS ON THE MARGINS OF SEPALS	BROADER SEPALS NONGLANDULAR UNICELLULAR HAIRS. NARROWER SEPALS 2-4 CELLED NONGLANDULAR HAIRS	BROADER SEPALS 1-3 CELLED NONGLANDULAR HAIRS. NARROWER SEPALS 4-CELLED NONGLANDULAR HAIRS	BROADER SEPALS 1-3 CELLED NONGLANDULAR HAIRS. NARROWER SEPALS 1-4 CELLED NONGLANDULAR HAIRS.	BROADER SEPALS 1-CELLED NONGLANDULAR HAIRS. NARROWER SEPALS 2 OR MORE CELLED NONGLANDULAR HAIRS	ALL FIVE SEPALS WITH 1-4 CELLED NONGLANDULAR HAIRS	ALL FIVE SEPALS WITH 1-4 CELLED NONGLANDULAR HAIRS
COROLLA	1-CELLED, LONG, NONGLANDULAR HAIRS ON INNER SURFACE	PRESENT, BUT WALLS SMOOTH AND PEG-LIKE PROJECTIONS ABSENT	PRESENT, BUT WALLS SMOOTH AND PEG-LIKE PROJECTIONS ABSENT	PRESENT, BUT WALLS SMOOTH AND PEG-LIKE PROJECTIONS ABSENT	PRESENT, BUT WALLS SMOOTH AND PEG-LIKE PROJECTIONS ABSENT	PRESENT, BUT WALLS SHRUNKEN AND PEG-LIKE PROJECTIONS PRESENT	PRESENT, WALLS SHRUNKEN BUT PEG-LIKE PROJECTIONS ABSENT
FOLIAGE LEAF		HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SIMILAR AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SIMILAR TO FLORAL LEAF	1. CELL WALLS OF UPPER EPIDERMIS MORE CONSPICUOUS 2. PAPILLA-LIKE TRICHOMES ON UPPER EPIDERMIS 3. LIGNIFIED HYPODERMIS ABSENT 4. CELLS OF LOWER EPIDERMIS LESS BEADED THAN THOSE OF FLORAL LEAVES	1. EPIDERMIS STRAIGHT WALLED, UNBEADED, CUTICLE UNSTRIATED, 2. MULTICELLULAR NONGLANDULAR HAIRS ON THE MARGINS

PLANT PART	TISSUE	7. THYMUS CARNOSUS BOISS.	8. THYMUS VILLOSUS LINN.	9. THYMUS HIRSUTUS BIEB.	10. THYMUS HETEROTRICHUS GRISEB.	11. THYMUS PECTINATUS FISCH.	12. THYMUS ZYGIS LINN.
FLORAL LEAF	UPPER AND LOWER EPIDERMIS	UPPER EPIDERMIS THICK WALLED, UNLIGNIFIED STRAIGHT-WAVY, RARELY BEADED, CUTICLE UNSTRIATED. LOWER EPIDERMIS WAVY, BEADED; STOMATA ABSENT ON UPPER SURFACE	CELL WALLS WAVY, SCARCELY BEADED, SCANTLY STRIATED; STOMATA UNEVENLY DISTRIBUTED	CELL WALLS, WAVY, BEADED, CUTICLE UNSTRIATED; STOMATA PRESENT	UPPER EPIDERMIS STRAIGHT, BEADED WALLS. LOWER EPIDERMIS-WAVY, BEADED WALLS, CUTICLE STRIATED; STOMATA PRESENT	CELL WALLS WAVY, BEADED, CUTICLE UNSTRIATED; STOMATA PRESENT	CELL WALLS WAVY, BEADED, CUTICLE OCCAS. STRIATED; STOMATA PRESENT
	EPIDERMAL HAIRS	TRICHOMES AND TRICHOME SCARS ABSENT ON UPPER SURFACE	TRICHOMES AND TRICHOME SCARS RARE	TRICHOMES AND TRICHOME SCARS PRESENT	TRICHOMES AND TRICHOME SCARS PRESENT	TRICHOMES AND TRICHOME SCARS PRESENT	TRICHOMES AND TRICHOME SCARS PRESENT. (ABSENT IN SOME SPECIMENS)
	HYPODERMIS	ABSENT	ABSENT	ABSENT	BOTH UPPER AND LOWER PRESENT, PARENCHYMATOUS	ABSENT	ABSENT
	PALISADE TISSUE	ONLY UPPER PALISADE PRESENT	PRONOUNCED PALISADE LACKING	ONLY UPPER PALISADE PRESENT	UPPER AND LOWER PALISADE PRESENT	UPPER AND LOWER PALISADE PRESENT	ONLY UPPER PALISADE PRESENT
	PALISADE NUMBER	9.9	9.3	11.0	10.6	14.0	15.2
	STOMATAL COUNT	9.5	NOT DETERMINED	17.0	9.9	NOT DETERMINED	9.2
STEM	EPIDERMAL HAIRS	TRICHOMES AND THEIR SCARS ALL OVER THE EPIDERMAL SURFACE	TRICHOMES AND THEIR SCARS ALL OVER THE EPIDERMIS ALTHOUGH INDICATIONS OF ROW ARRANGEMENT	TRICHOMES AND THEIR SCARS ARRANGED IN ROWS ON EPIDERMAL SURFACE	TRICHOMES AND THEIR SCARS SCATTERED ALL OVER THE EPIDERMAL SURFACE	TRICHOMES AND THEIR SCARS SCATTERED ALL OVER THE EPIDERMAL SURFACE	TRICHOMES ARRANGED IN ROWS

PLANT PART	TISSUE	7	8	9	10	11	12
CALYX	EPIDERMIS OF OUTER TUBULAR REGION	INTERRIB REGION WITHOUT FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITHOUT FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITHOUT FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITH FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITHOUT FLUTED OR STRIATED PAPILLAE	INTERRIB REGION WITHOUT FLUTED OR STRIATED PAPILLAE
	OUTER RIB REGION	FIBERS IN THE RIB REGION PRESENT	FIBERS IN THE RIB REGION ABSENT	FIBERS IN THE RIB REGION PRESENT	FIBERS IN THE RIB REGION PRESENT	FIBERS IN THE RIB REGION PRESENT	FIBERS IN THE RIB REGION PRESENT
	PALISADE LIKE CELLS IN DIVIDED REGION	ROUND IN SURFACE VIEW	IRREGULAR IN SHAPE, WITH INTERCELLULAR SPACES	IRREGULAR IN SHAPE, WITH INTERCELLULAR SPACES	ROUND IN SURFACE VIEW	IRREGULAR IN SHAPE, WITH INTERCELLULAR SPACES	ROUND IN SURFACE VIEW
	HAIRS ON THE MARGINS OF SEPALS	BROADER SEPALS-FEW NONGLANDULAR BUT SMALL GLANDULAR HAIRS, NARROWER SEPALS-1-3 CELLED NONGLANDULAR HAIRS	ALL FIVE SEPALS WITH 1-4 CELLED NONGLANDULAR HAIRS	ALL FIVE SEPALS WITH 1-4 CELLED NONGLANDULAR HAIRS	ALL FIVE SEPALS WITH 1-4 CELLED NONGLANDULAR HAIRS	ALL FIVE SEPALS WITH 1-4 CELLED NONGLANDULAR HAIRS	BROADER SEPALS-PAPILLA LIKE NONGLANDULAR HAIRS, NARROWER SEPALS-1-4 CELLED NONGLANDULAR HAIRS.
COROLLA	1-CELLED LONG, NONGLANDULAR HAIRS ON INNER SURFACE	PRESENT, WALLS SHRUNKEN BUT PEG-LIKE PROJECTIONS ABSENT	PRESENT, WALLS SHRUNKEN BUT PEG-LIKE PROJECTIONS ABSENT	PRESENT, WALLS SHRUNKEN BUT PEG-LIKE PROJECTIONS ABSENT	ABSENT	ABSENT	ABSENT
FOLIAGE LEAF		HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF	HISTOLOGICAL STRUCTURES SAME AS IN FLORAL LEAF

STUDIES OF THE GENUS THYMUS

PART X

Histological Key for the Identification of Certain Thymus Species

By Ikram Hassan * and M. S. Dunn **

IN papers I and III, the study of the transverse sections of the floral leaves of Thymus vulgaris Linn., Thymus Serpyllum Linn., Thymus Chamaedrys Fries, and Thymus Herba-barona Loisel was not attempted. During the examination of subsequent Thymus species, it became increasingly apparent that the histological structures of the floral leaves as seen in transverse section was of importance in comparing the different species.

Since the histological construction of transverse sections of floral leaves plays a part in the construction and use of the histological key to the species which follows, transverse sections of Thymus vulgaris Linn., Thymus Serpyllum Linn., Thymus Chamaedrys Fries, and Thymus Herba-barona, were made and drawings of these are shown for the sake of completeness in figure I.

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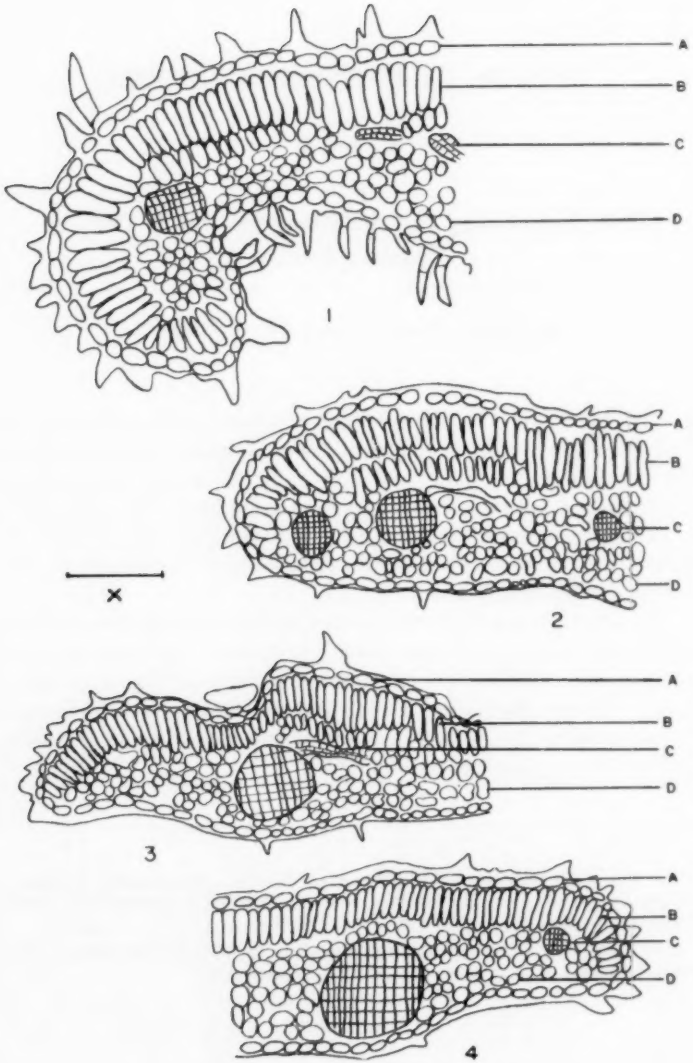
** Professor of Biology and Director of the Department of Biology, Philadelphia College of Pharmacy and Science, Philadelphia.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KEY TO THE HISTOLOGICAL IDENTIFICATION OF THYMUS SPECIES

A. Hypodermis present in the floral leaf:

B. Hypodermis lignified:

Palisade-like cells unlignified, thick walled (in calyx region) . . . Thymus capitatus Hoffmagg. and Link.

BB. Hypodermis unlignified:

Palisade-like cells thin walled, parenchymatous (in calyx region) . . . Thymus heterotrichus Griseb.

AA. Hypodermis absent in the floral leaf:

B. Stem trichomes in four distinct rows:

C. Cells with fluted or striated papillae in the epidermis of the interrib region of calyx present.

Broader sepals with 1-3 celled marginal nonglandular hairs, and the narrower sepals with 1-4 celled marginal nonglandular hairs . . . Thymus Chamaedrys Fries.

CC. Cells with fluted or striated papillae in the interrib region of the calyx absent.

D. Palisade cells in floral leaf lacking . . . Thymus villosus Linn.

DD. Palisade cells in the floral leaf 1-2 layered . . . Thymus hirsutus Bieb.

←

FIGURE I

TRANSVERSE SECTION OF THE FLORAL LEAVES OF:

1. Thymus vulgaris Linn.
2. Thymus Serpyllum Linn.
3. Thymus Chamaedrys Fries.
4. Thymus Herba-barona Loisel.

A. Upper epidermis. B. Palisade tisue. C. Vein cut transversely or obliquely. D. Spongy tissue.

Camera lucida drawings (semidiagrammatic). Scale × = 34 microns.

BB. Stem trichomes scattered over the surface not in observable rows.

C. Fluted or striated papillae in the interrib region of the calyx present.

D. Broader sepals of calyx with 1-celled marginal hairs; narrower sepals of calyx with 2 or more celled marginal hairs . . . Thymus Herba-barona Loisel.

DD. Broader sepals of calyx with more than one celled marginal hairs; narrower sepals of calyx with 1-4 celled marginal hairs.

E. Floral leaf with trichomes . . . Thymus striatus Vahl.

EE. Floral leaf almost devoid of trichomes . . . Thymus Serpyllum Linn.

CC. Fluted papillae in the interrib region of the calyx absent.

D. Broader sepals of calyx with small glandular hairs on the margins . . . Thymus carnosus Boiss.

DD. Broader sepals of calyx without glandular hairs on the margins.

E. Only upper palisade tissue present in the floral leaf . . . Thymus vulgaris Linn.

EE. Upper and lower palisade tissue present in floral leaf . . . Thymus pectinatus Fisch.

ADDENDUM

Hassan, I., and Dunn, M. S., "Studies of the Genus Thymus, Part I," *Amer. J. Pharm. 129:* p. 370. Magnification of Fig. 5, 5 should be described as approx. 550×.

SELECTED ABSTRACTS

The Stability of an Ophthalmic Solution of Resorcinol. Morch, J. and Morch, K. *Dansk Tidsskrift for Farmaci 32:73* (1958). The Danish Pharmacopoeia contains an ophthalmic solution (eye drops) containing resorcinol 1 per cent and sodium chloride 0.6 per cent in distilled water. The preparation may not be heat sterilized and may not be stored for more than 3 months, since the resorcinol is readily oxidized with the development of a reddish color. The authors chromatographically separated the oxidation products from this preparation into four different components. A spectrophotometric method for the analysis of the eye drops was described, the non-oxidized portion of the resorcinol being estimated from the extinction at 274 mu. The procedure cannot be used in strongly colored solutions.

Stability studies on the resorcinol eye drops showed that the addition of 0.05 per cent sodium pyrosulfite (sodium metabisulfite) prevented discoloration of the solution even after autoclaving at 120° C. for 20 minutes. Sodium citrate was also added as a buffer to prevent a decrease in pH, in a concentration sufficient to make the solution isoosmotic. Such a solution was found to be stable for one year in small, rubber capped vials. The author stated that the effect of the sodium metabisulfite was only cosmetic if the decrease in pH was prevented by the addition of a buffer.

Since it is known that traces of copper ion catalyze the oxidation of resorcinol, the authors investigated the effect of the addition of chelating agents to the official eye drops. Cupric ions were added in the form of cupric sulfate. Thiourea, normal oxyquinoline sulfate, and disodium ethylenediaminetetraacetate all showed good results as stabilizers in optimum concentrations of 0.01, 0.005 and 0.005 per cent, respectively. The pH of the official solution was not changed by the addition of the stabilizers. None of the stabilizers appeared to be markedly superior. Oxyquinoline sulfate was more effective in higher than the above optimum concentration but the solution was yellow in color due to the stabilizer. Oxyquinoline sulfate also has the advantage of being a bacteriostatic agent. The sodium ethylenediaminetretraacetate appeared to prevent the development of color somewhat more completely.

The Effect of Heat on Hydrophilic Emulsifiers and Emulsions. Benerito, R. R., and Singleton, W. S. *Am. Perfumer 69:37* (1957). The heat sterilization of oil-in-water emulsions for intravenous administration imposes a severe physical strain on the emulsion. At least two factors affect the stability of emulsions to heat sterilization. First the hydrophilic portion of the emulsifier must maintain an appreciable degree of water solubility at the temperature of sterilization. Secondly, the hydrogen bonds linking the emulsifier to water molecules are relatively weak bonds, apparently most such bonds have an energy of dissociation of about 7 kcal./mole. Simply the kinetic energy of motion at the sterilization temperature (121° C.) is often sufficient to break such bonds.

The authors reported a study of the effect of heat upon the solubility of a series of non-ionic emulsifiers. As the temperature of a solution of such emulsifiers was increased, a point was reached where the hydrogen bonding with water was broken. At this point the solution became a turbid dispersion. In general, it was found that the temperature at which solubility inversion occurred increased as the weight percentage of polyoxyethylene groups increased. For example, the variation in limit of solubility of the polyoxyethylene glycol lauryl ester type emulsifiers was from insoluble at room temperature to soluble up to 92° C., as the weight percentage of polyoxyethylene groups increased from 52 to 91 per cent. Widely different inversion temperatures were found with some of the other ester types studied. In general, the amine type of emulsifier was more soluble than the amide, which in turn was more soluble than the ester type. Polyethylene-propylene oxide had the longest solubility range of the emulsifiers studied.

Several emulsions containing 15 per cent by weight of a refined, bleached, and deodorized sesame oil and 1 per cent of an emulsifier were prepared. It was found that a pressure of about 3500 p.s.i. was required with several recycles to attain a particle size of 0.5 micron, the maximum particle size suitable for intravenous administration. These emulsions were prepared with emulsifiers which had shown the higher temperature solubilities, and then autoclaved at 121° C. for 10 minutes. An increase in particle size or an appearance of two phases in emulsions prepared with emulsifiers which underwent solubility inversion below 85° C. was observed. The combination of high temperature and extreme mechanical shear caused by homogenization

at high pressure as well as the high temperature of sterilization caused particle-size growth. In general, it appeared that emulsifiers required approximately 70 per cent by weight of polyoxyethylene groups in order to withstand homogenization and sterilization. Emulsions prepared with emulsifiers having inversion temperatures above 85° C. maintained, generally, a low particle size on autoclaving and did not separate.

A few emulsions were prepared using a combination of a hydrophilic and a lipophilic emulsifier. Better emulsions with respect to particle size were obtained. For example, an emulsion containing a polyoxyethylene lauryl alcohol as the only emulsifier showed no separation of phases on autoclaving, but the particle size ranged up to 2 microns. By the addition of a more lipophilic emulsifier, polyoxyethylene sorbitol triglyceride, the particle size was uniformly about 0.7 micron. Apparently, a more stable bond between the oil and water phases was obtained, and the change in free energy of interfacial surface formation was less when two emulsifiers were used.

The Stability of Colchicine in Solution. Wood, D. R. *The Pharm J. 178:*188 (1957). Colchicine readily forms colchiceine on heating with dilute acids or alkalies. This decomposition product is similar, chemically, to colchicine but its pharmacologic activity is much lower.

In order to determine whether or not colchicine decomposes to colchiceine in neutral or slightly alkaline solutions, the author prepared a solution containing 0.002 per cent colchicine base in distilled water and another in potassium bicarbonate solution having a pH of 8.1. The solutions were then allowed to stand and studied spectrophotometrically. There was no evidence of decomposition in either solution over a period of 18 days.

Another pair of solutions in the same vehicles but containing 0.1 per cent colchicine were tested qualitatively for the presence of colchiceine by the development of a green color in chloroform upon the addition of ferric chloride. No significant color development occurred in either solution during a period of two months.

The author concluded that no significant hydrolysis of colchicine to colchiceine occurred in solutions having a neutral or slightly alkaline pH.

The Heat Stabilizing Effects of Isoniazid on Dihydrostreptomycin and Streptomycin. Berczeller, A., and Frank, G. *Antibiot. and Chemother. 8:*309 (1958). The stabilizing effects of isoniazid on solutions of dihydrostreptomycin (DHSM) and streptomycin (SM) was investigated. The solutions contained 500 mg./ml. DHSM or SM and 120 mg./ml. (approximately equimolar concentration with the antibiotics), 50, 25, 12.5, 5, 2.5 or 1 mg./ml. isoniazid. One series of these solutions was autoclaved and the other stored at refrigerator temperature. The solutions were then all assayed for microbiological activity and by infrared spectroscopy for chemical components. They were also observed for appearance.

After autoclaving, solutions containing DHSM or SM but with no isoniazid were black in color and muddy in appearance and they had lost all antibacterial activity. Solutions containing equimolar concentrations of isoniazid remained clear and lost none of their antibacterial activity after autoclaving. Lower concentrations of isoniazid provided decreasing protection to the antibiotics during autoclaving as the concentration of isoniazid decreased. Thus, isoniazid was found to be a potent stabilizer of streptomycin and dihydrostreptomycin in solution, providing stability even during autoclaving at 121° C. for 30 minutes.

Infrared spectroscopic study of the constituents of these solutions gave some indication of the mechanism by which isoniazid provided protection to these antibiotics. After autoclaving the SM-isoniazid mixture, a new compound, streptomycylidene isonicotinyl hydrazine was formed. This might account for the stability toward autoclaving. However, no compound is formed in the DHSM-isoniazid mixture. In the heat-deteriorated spectrum of DHSM alone, the prevailing changes noted were oxidative changes with loss of hydroxyl groups and appearance of carboxyl groups. Thus, it was suggested that the hydrazine moiety of isoniazid might act as a reducing agent. Also, the pyridine moiety of isoniazid may act as a buffer, since the autoclaved mixture was found to have a pH of 5.6 to 5.9 while autoclaved DHSM alone had a pH of 1.4 to 1.8.

The addition of isoniazid to solutions of SM and DHSM has the double advantage of providing a stabilizer and a therapeutic agent.

BOOK REVIEWS

Biochemical Preparations. Volume 5. David Shemin, Editor-in-chief. ix + 115 pp. 1957. John Wiley and Sone, Inc., New York 16, N. Y. Price $4.75.

This recent volume is similar in style to *Organic Syntheses* and the previous editions of this work. Eighteen basic preparative methods are presented and two separation techniques—of the nucleotides of ribonucleic acid and 5'-deoxyribonucleotides—are elegantly described. In most of the preparations a method of determination of purity, essential in biochemical materials, is discussed. Also included are references to compounds of biochemical interest which have appeared in *Organic Syntheses,* through volume 37. The index is cumulative for the first five volumes of the series. Naturally, the book is a must for any chemist with biochemical interests.

A. R. GENNARO

Biochemistry of Some Peptide and Steroid Antibiotics. E. P. Abraham. xi + 96 pp. John Wiley & Sons, Inc., New York 16, N. Y., 1957. Price $3.00.

This is the second volume of the annual CIBA lectures in microbial chemistry. The three chapters are concerned with the Bacitracins, Cephalosporins, and their structural and functional relationships to other antibiotics. It is a well-written, pocket-sized book which is an adventure into the investigations of the structural, biochemical, antibiotic, and chemotherapeutic aspects of the two series of antibiotics. A book of this sort elegantly describes the fascination of researches into the biological and chemical sciences and will make for exciting reading for anyone with an understanding of the basic difficulties in opening new frontiers in any realm of science.

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